

Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1. *(currently amended)* A conjugate comprising ~~one or more~~ a bioactive ~~components~~ component covalently attached to at least one linear or branched polyalkylene glycol, wherein each said polyalkylene glycol is attached to ~~one of~~ said bioactive ~~components~~ component at a single site on the polyalkylene glycol and said polyalkylene glycol, if linear, has a hydroxyl group at a its distal terminus ~~and or~~, if branched, has a hydroxyl group at every distal terminus.

2. *(currently amended)* The conjugate of claim 1, wherein said conjugate is reduced or substantially reduced in antigenicity compared to a conjugate comprising the same bioactive ~~component(s)~~ component linked at the same site or sites on the bioactive ~~component(s)~~ component to the same number of polyalkylene glycols of the same size and the same linear or branched structure containing one or more distal terminal alkoxyl groups.

3. *(original)* The conjugate of claim 1, wherein said linear or branched polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol) and a copolymer of ethylene oxide and propylene oxide.

4. *(original)* The conjugate of claim 3, wherein said linear or branched polyalkylene glycol is a poly(ethylene glycol) ("PEG").

5. *(currently amended)* The conjugate of claim 1, wherein the attachment of said polyalkylene glycol to said bioactive ~~component(s)~~ component is carried out

using a reactive derivative of at least one polyalkylene glycol selected from the group consisting of linear dihydroxyPEGs (“PEG diols”), hydroxyPEG-monoacetals and hydroxyPEG-monoacids.

6. *(currently amended)* The conjugate of claim 1, wherein the attachment of said polyalkylene glycol to said bioactive ~~component(s)~~ component is carried out using a reactive derivative of hydroxyPEG selected from the group consisting of a monoaldehyde, a monoester of a monoacid, a monoamine, a monothiol, a monodisulfide, a monobromophenyl carbonate, a monochlorophenyl carbonate, a monofluorophenyl carbonate, a mononitrophenyl carbonate, a monocarbonylimidazole, a monohydrazide, a monocarbazate, a moniodoacetamide, a monomaleimide, a monoorthopyridyl disulfide, a monooxime, a monophenyl glyoxal, a monothiazolidine-2-thione, a monothioester, a monotriazine and a monovinylsulfone.

7. *(original)* The conjugate of claim 1, wherein said polyalkylene glycol has a molecular weight of from about 1,000 Daltons (1 kDa) to about 100,000 Daltons (100 kDa).

8. *(original)* The conjugate of claim 7, wherein said polyalkylene glycol has a molecular weight of from about 2 kDa to about 60 kDa.

9. *(original)* The conjugate of claim 8, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 2 kDa to about 30 kDa.

10. *(original)* The conjugate of claim 9, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 5 kDa to about 20 kDa.

11. (*original*) The conjugate of claim 8, wherein said polyalkylene glycol has a molecular weight of from about 10 kDa to about 20 kDa.
12. (*withdrawn*) The conjugate of claim 11, wherein said polyalkylene glycol has a molecular weight of about 12 kDa.
13. (*original*) The conjugate of claim 8, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 60 kDa.
14. (*original*) The conjugate of claim 13, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 22 kDa.
15. (*original*) The conjugate of claim 14 wherein said polyalkylene glycol has a molecular weight of about 20 kDa.
16. (*withdrawn*) The conjugate of claim 13, wherein said polyalkylene glycol has a molecular weight of about 27 kDa to about 33 kDa.
17. (*original*) The conjugate of claim 1, wherein said conjugate comprises from about one to about 100 strands of said polyalkylene glycol.
18. (*original*) The conjugate of claim 17, wherein said conjugate comprises from about one to about five strands of said polyalkylene glycol.
19. (*original*) The conjugate of claim 18, wherein said conjugate comprises about one or about two strands of said polyalkylene glycol.
20. (*original*) The conjugate of claim 17, wherein said conjugate comprises from about five to about 100 strands of said polyalkylene glycol.

21. (*previously presented*) The conjugate of claim 1, wherein said polyalkylene glycol is selected from the group consisting of a monohydroxyPEG-acid and a dihydroxyPEG-acid.

22. (*canceled*)

23. (*original*) The conjugate of claim 5, wherein said polyalkylene glycol is a reactive derivative of said linear dihydroxyPEG.

24. (*currently amended*) The conjugate of claim 5, wherein said polyalkylene glycol is a reactive derivative of said ~~hydroxyPEG-monocarboxylic acid~~ hydroxyPEG-monoacid.

25. (*original*) The conjugate of claim 1, wherein said bioactive component is selected from the group consisting of a peptide, a protein, a glycoprotein, an organic compound, an amine-containing compound, a carboxyl-containing compound, a hydroxyl-containing compound and a thiol-containing compound.

26. (*original*) The conjugate of claim 25, wherein said bioactive component is selected from the group consisting of a peptide, a protein and a glycoprotein.

27-34. (*canceled*).

35. (*original*) The conjugate of claim 26, wherein said peptide, protein or glycoprotein is an allergen.

36. (*withdrawn - currently amended*) The conjugate of claim 1, wherein said bioactive ~~compound~~ component is a taxane or a derivative thereof.

37. *(withdrawn - currently amended)* The conjugate of claim 1, wherein said bioactive ~~compound~~ component is an antibiotic or a derivative thereof.

38. *(original)* A pharmaceutical composition comprising the conjugate of claim 1 and a pharmaceutically acceptable excipient or carrier.

39. - 58. *(canceled)*

59. *(currently amended)* A conjugate comprising ~~one or more~~ a bioactive ~~components~~ component covalently attached to at least one linear or branched polyalkylene glycol activated at only one terminus ("a ~~monoactivated~~ monofunctionally activated polyalkylene glycol") produced by a method comprising:

(a) obtaining a polyalkylene glycol that has a hydroxyl group at every terminus ~~does not contain any end group that is a stably linked alkoxyl group;~~

(b) optionally, prior to the conversion of the polyalkylene glycol of (a) to a monofunctionally activated polyalkylene glycol, protecting all except one of the ~~end~~ hydroxyl groups by the addition of one or more removable blocking groups, such as *t*-butoxyl group(s), aryloxyl group(s) or triphenylmethyl group(s) ("trityl group(s)");

(c) producing a monofunctionally activated derivative of said polyalkylene glycol by reacting said polyalkylene glycol with a derivatizing compound or compounds under conditions such that said polyalkylene glycol is derivatized with a single derivatizing group at ~~an end~~ a hydroxyl group that does not contain said removable blocking group or groups;

(d) if a blocking group was added to protect the ~~end~~ hydroxyl group(s) in (b)-~~above~~, removing said blocking group without removing the activating group attached in (c)-~~above~~, to produce a monofunctionally activated polyalkylene glycol wherein the distal terminus or distal termini are hydroxyl groups; and

(e) contacting said monofunctionally activated polyalkylene glycol with at ~~least one~~ a bioactive component, under conditions that favor the covalent binding of said monofunctionally activated polyalkylene glycol to said bioactive component, or

(f) alternatively, performing (e)-~~above~~ prior to performing (d)-~~above~~.

60. (*currently amended*) The conjugate of claim 59, wherein said conjugate is reduced or substantially reduced in antigenicity compared to a conjugate comprising a polyalkylene glycol containing at least one alkoxyl group at a distal terminus and the same bioactive component linked at the same site or sites on the bioactive component to the same number of molecules of polyalkylene glycol of the same size and the same linear or branched structure.

61. (*original*) The conjugate of claim 59, wherein said polyalkylene glycol is selected from the group consisting of a poly(ethylene glycol) and a copolymer of ethylene oxide and propylene oxide.

62. (*original*) The conjugate of claim 59, wherein the polyalkylene glycol component is selected from the group consisting of a linear poly(ethylene glycol) and a branched poly(ethylene glycol).

63. (*original*) The conjugate of claim 59, wherein each said polyalkylene glycol has a molecular weight of from about 1 kDa to about 100 kDa.

64. (*original*) The conjugate of claim 63, wherein said polyalkylene glycol has a molecular weight of from about 2 kDa to about 60 kDa.

65. (*original*) The conjugate of claim 64, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 2 kDa to about 30 kDa.

66. (*original*) The conjugate of claim 65, wherein said polyalkylene glycol has two branches, each with a molecular weight of from about 5 kDa to about 20 kDa.

67. (*original*) The conjugate of claim 64, wherein said polyalkylene glycol has a molecular weight of from about 10 kDa to about 20 kDa.

68. (*withdrawn*) The conjugate of claim 67, wherein said polyalkylene glycol has a molecular weight of about 12 kDa.

69. (*original*) The conjugate of claim 64, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 60 kDa.

70. (*original*) The conjugate of claim 69, wherein said polyalkylene glycol has a molecular weight of from about 18 kDa to about 22 kDa.

71. (*original*) The conjugate of claim 70, wherein said polyalkylene glycol has a molecular weight of about 20 kDa.

72. (*withdrawn*) The conjugate of claim 69, wherein said polyalkylene glycol has a molecular weight of about 27 kDa to about 33 kDa.

73. (*original*) The conjugate of claim 59, wherein said conjugate comprises from one to about 100 strands of said polyalkylene glycol.

74. *(original)* The conjugate of claim 73, wherein said conjugate comprises from about one to about five strands of said polyalkylene glycol.

75. *(original)* The conjugate of claim 74, wherein said conjugate comprises about one or about two strands of said polyalkylene glycol.

76. *(original)* The conjugate of claim 73, wherein said conjugate comprises about five to about 100 strands of said polyalkylene glycol.

77. *(previously presented)* The conjugate of claim 59, wherein said monofunctionally activated polyalkylene glycol used in the synthesis of said conjugate is selected from the group consisting of a hydroxyPEG-monoaldehyde and a reactive ester of a hydroxyPEG-monoacid.

78. *(canceled)*

79. *(previously presented)* The conjugate of claim 59, wherein said monofunctionally activated polyalkylene glycol used in its synthesis is derived from a linear dihydroxyPEG.

80. *(previously presented)* The conjugate of claim 59, wherein said bioactive component is selected from the group consisting of a peptide, a protein, a glycoprotein, an organic compound, an amine-containing compound, a carboxyl-containing compound, a hydroxyl-containing compound and a thiol-containing compound.

81. *(original)* The conjugate of claim 80, wherein said bioactive component is selected from the group consisting of a peptide, a protein and a glycoprotein.

82-89. *(canceled)*.

90. *(original)* The conjugate of claim 81, wherein said peptide, protein or glycoprotein is an allergen.

91. *(withdrawn)* The conjugate of claim 59, wherein the bioactive compound is a taxane or a derivative thereof.

92. *(withdrawn)* The conjugate of claim 59, wherein said bioactive compound is an antibiotic or a derivative thereof.

93. *(original)* A pharmaceutical composition comprising the conjugate of claim 59 and a pharmaceutically acceptable excipient or carrier.

94. *(original)* A kit comprising the conjugate of claim 1.

95. *(original)* A kit comprising the pharmaceutical composition of claim 38.

96. *(original)* A kit comprising the conjugate of claim 59.

97. - 108. *(canceled)*

109. *(previously presented)* The conjugate of claim 21, wherein said dihydroxyPEG-acid is dihydroxyPEG-lysine.

110. *(new)* The conjugate of claim 26, wherein said peptide or protein or glycoprotein is selected from the group consisting of an enzyme, a serum protein, a serum glycoprotein, a blood cell protein, a pigmentary protein, hemoglobin, a viral protein, a peptide hormone, a protein hormone, a glycoprotein hormone, a hypothalamic releasing factor, a cytokine and a growth factor.

111. *(new)* The conjugate of claim 110, wherein said serum protein is selected from the group consisting of an albumin, an immunoglobulin and a blood clotting factor.

112. (new) The conjugate of claim 110, wherein said peptide hormone or protein hormone or glycoprotein hormone is selected from the group consisting of an antidiuretic hormone, chorionic gonadotropin, luteinizing hormone, follicle-stimulating hormone, insulin, prolactin, a somatomedin, growth hormone, thyroid-stimulating hormone and a placental lactogen.

113. (new) The conjugate of claim 110, wherein said growth factor is selected from the group consisting of a colony-stimulating factor, an epidermal growth factor, erythropoietin, a fibroblast growth factor, an insulin-like growth factor, a transforming growth factor, a platelet-derived growth factor, a nerve growth factor, a hepatocyte growth factor, a neurotrophic factor, a ciliary neurotrophic factor, a brain-derived neurotrophic factor, a glial-derived neurotrophic factor and a bone morphogenic peptide.

114. (new) The conjugate of claim 110, wherein said cytokine is selected from the group consisting of a lymphokine, an interleukin, an interferon, a tumor necrosis factor, a leukemia inhibitory factor and thrombopoietin.

115. (new) The conjugate of claim 110, wherein said enzyme is selected from the group consisting of a carbohydrate-specific enzyme, a proteolytic enzyme, an oxidoreductase, a transferase, a hydrolase, a lyase, an isomerase and a ligase.

116. (new) The conjugate of claim 115, wherein said oxidoreductase is a uricase.

117. (new) The conjugate of claim 115, wherein said proteolytic enzyme is a plasminogen activator.

118. (*new*) The conjugate of claim 81, wherein said peptide or protein or glycoprotein is selected from the group consisting of an enzyme, a serum protein, a serum glycoprotein, a blood cell protein, a pigmentary protein, hemoglobin, a viral protein, a peptide hormone, a protein hormone, a glycoprotein hormone, a hypothalamic releasing factor, a cytokine and a growth factor.

119. (*new*) The conjugate of claim 118, wherein said serum protein is selected from the group consisting of an albumin, an immunoglobulin and a blood-clotting factor.

120. (*new*) The conjugate of claim 118, wherein said peptide hormone or protein hormone or glycoprotein hormone is selected from the group consisting of an antidiuretic hormone, chorionic gonadotropin, luteinizing hormone, follicle-stimulating hormone, insulin, prolactin, a somatomedin, growth hormone, thyroid-stimulating hormone and a placental lactogen.

121. (*new*) The conjugate of claim 118, wherein said growth factor is selected from the group consisting of a colony-stimulating factor, an epidermal growth factor, erythropoietin, a fibroblast growth factor, an insulin-like growth factor, a transforming growth factor, a platelet-derived growth factor, a nerve growth factor, a hepatocyte growth factor, a neurotrophic factor, a ciliary neurotrophic factor, a brain-derived neurotrophic factor, a glial-derived neurotrophic factor and a bone morphogenic peptide.

122. (*new*) The conjugate of claim 118, wherein said cytokine is selected from the group consisting of a lymphokine, an interleukin, an interferon, a tumor necrosis factor, a leukemia inhibitory factor and thrombopoietin.

123. (new) The conjugate of claim 118, wherein said enzyme is selected from the group consisting of a carbohydrate-specific enzyme, a proteolytic enzyme, an oxidoreductase, a transferase, a hydrolase, a lyase, an isomerase and a ligase.

124. (new) The conjugate of claim 123, wherein said oxidoreductase is a uricase.

125. (new) The conjugate of claim 123, wherein said proteolytic enzyme is a plasminogen activator.

126. (new) The conjugate of claim 110, wherein said growth factor is a colony-stimulating factor.

127. (new) The conjugate of claim 126, wherein said colony-stimulating factor is a granulocyte-macrophage colony-stimulating factor (GM-CSF).

128. (new) The conjugate of claim 127, wherein said GM-CSF is covalently attached to one linear or branched polyalkylene glycol molecule that, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

129. (new) The conjugate of claim 127, wherein said GM-CSF is covalently attached to two linear or branched polyalkylene glycol molecules each of which, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

130. (new) The conjugate of claim 118, wherein said growth factor is a colony-stimulating factor.

131. (*new*) The conjugate of claim 130, wherein said colony-stimulating factor is a GM-CSF.

132. (*new*) The conjugate of claim 131, wherein said GM-CSF is covalently attached to one linear or branched polyalkylene glycol molecule that, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

133. (*new*) The conjugate of claim 131, wherein said GM-CSF is covalently attached to two linear or branched polyalkylene glycol molecules each of which, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

134. (*new*) The conjugate of claim 113, wherein said growth factor is erythropoietin.

135. (*new*) The conjugate of claim 134, wherein said erythropoietin is covalently attached to one linear or branched polyalkylene glycol molecule that, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

136. (*new*) The conjugate of claim 134, wherein said erythropoietin is covalently attached to two linear or branched polyalkylene glycol molecules each of which, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

137. (*new*) The conjugate of claim 121, wherein said growth factor is erythropoietin.

138. (*new*) The conjugate of claim 137, wherein said erythropoietin is covalently attached to one linear or branched polyalkylene glycol molecule that, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.

139. (*new*) The conjugate of claim 137, wherein said erythropoietin is covalently attached to two linear or branched polyalkylene glycol molecules each of which, if linear, has a hydroxyl group at its distal terminus, or, if branched, has a hydroxyl group at every distal terminus.